

**Conference Proceedings**  
***PRE-ATTACK PANEL: Prevention and Deterrence***

**Guest Luncheon Speaker**

**Dr. Joshua Lederberg, Rockefeller University**  
***The Diversity of Bio Weapons***

Thank you very much and especially for that introduction. I really have to update that page and in particular make sure that there's a plug for the book I edited: "Biological weapons, containing the threat" published by the MIT Press. A number of brilliant contributors have converged and give you a very deep background for much of the discussion you've had today and in particular for my own remarks.

The title that I had agreed to here was "diversity of biological weapons". I arrived here this morning from New York -- just in time to get some sense and feeling of the remainder of the discussion and of the group in attendance; I decided to shift gear a little bit, and pursue how we might be dealing with present and future technologies for bio attack and defense.

And I'll say just a word about defense. A lot of very clever people are working on diagnostics. We will be hearing more about the very innovative approaches that are being developed, (a good part in the national laboratories) for the rapid sensing and diagnosis of infectious agents in the environment and from tissue and blood samples from exposed individuals. That's absolutely critical to recognizing that an attack has happened, that it might be going on, and as well as for the care and treatment of those at risk. Even so, for the next few years, we'd be very lucky to be able to detect a clandestine anthrax or smallpox attack before a substantial number of people started showing symptoms, and that would be squandering 2 or 3 days of very precious time absolutely crucial to the management of the consequences. We perhaps put too much stress on an acute incident, an explosion, a compelling notice that something really awful has happened. That would entail the involvement of emergency responders, many of whom are here. The avenue of heroic efforts of salvage and refuge is a carry-over from the use of explosives, and would apply in some degree to chemical attacks. But no shrewd user of a BW weapon is going to give you that opportunity. The "incident" will be people accumulating illness, disease, death. Finally, then the evidence may become overwhelming that this is out of the ordinary, and the public health system will begin to take hold. So a very important aspect for defense against BW is to adopt the correct level of paranoia, when possibly random fluctuations of the incidence of disease, an epidemic of a mild, or not so mild, influenza starts bringing people to the hospitals. Or even speculating that a new disease like West Nile now transmitted by mosquitoes in New York, and the crows falling at our feet -- might that be a BW attack or not? We'll never know for sure although that's an extremely improbable explanation. So very different scenarios than often come under the heading of incident management would apply under those circumstances; they're going to take even more advanced tools for diagnosis; and sophisticated organizational approach; alertness and worry about a lot of false alarms. But we must not ignore the next alarm that comes along which might not be so false. Advances in diagnosis will march on, depending on specific diseases. I think we'll beat the bacterial infections, and we'll recover our overwhelming defense capability even in the face of the waves of antibiotic resistance that bacteria have generated out of careless use of antibiotics. The industry is coming around to developing new antibacterial agents. If we're a little bit smarter this time around about how they're deployed, we can recover some confidence that we can deal with almost any bacterial infection with a high degree of efficiency. Diagnosis will be important in order to know which agents to use.

I wish I could be quite that optimistic about viral infections for which therapeutic measures are few and far between. Our frustration in dealing with AIDS is an example of that, which has had the most concentrated effort in history at the development of therapeutics. At the moment the best that can be said is that we have some stop gaps that will slow up the progress of the disease and afford an extra few years of life in a condition that's already very chronic. And perhaps there will be some improvement if there's renewed investment in dealing with other virus diseases. That's the only approach that I can see as being feasible on a strategic level in dealing with smallpox. Are we going to persuade ourselves or others that we ought to, gain, revaccinate the entire world's population? Once you stop and think about the implications on doing this on a merely regional or national level without the world being involved in this, you'll see why it's an all or none global decision. But if we could have therapeutics that could deal with a smallpox attack once it had started, so it's not so inevitably lethal as it offers to be at the present time, that would greatly alter the picture. The same might apply for preparedness for a broad range of other viral attacks. So it's a little bit chancy but one could be moderately optimistic about the pace of development of therapeutic management measures coming from the technologies of the next 5 to 10 years. Nevertheless, the offense will be preponderant as we understand infectious disease in greater and greater depth: our ability to conduct DNA analysis sequencing, moving bits of DNA from one organism to another, genetic engineering as it is applied to very beneficent purposes.

These also do open a Pandora's box of limitless dimensions. It is easy to imagine organisms that might be concocted either to promote unlimited spread, or even, I hate to say it, of being able to target particular population sectors, which is more fearful to some than the city at large. These might be differentiated to a very limited degree by their genetic background, but more likely by diet, other infections, geography, conditions of life -- as applies also to natural disease. It's just built in that the knowledge that is being accumulated in the basic biochemistry of infection is going to make it a lot easier to perfect biological weapons than to build defenses against them.

We have probably already had sufficient arousal about dealing with the purely technical issues. There has also been considerable commotion about the organizational issues and it's gratifying to hear about the cooperation that's been elicited so far. We have a long way to go. One way of expressing my level of concern is that the technologies are so accessible. Growing anthrax is as easy as baking a pie, finding anthrax seed is not that tough. Outbreaks of it occur in cattle from time to time. Any large farm community will know some field where some cow has died of it and where you could recover anthrax from the soil with a little digging around. You don't have to go to stock culture collections or the laboratories in order to find many of the worst of these diseases. They are, after all, natural phenomena and one can, as the microbiologists often do, recover the infectious agents from those sources or from sewage. But that says that high school students are going to have to be added to our roster of potential sources of threat. Recall the Columbine high school massacre. These youngsters are a lot more exploratory, perhaps even a lot smarter, than they will be 10-15 years later down stream--that's just a fact of developmental biology. Thousands of high school kids are doing biotechnology as part of their high school research projects, at a level that is quite sophisticated enough for devising brand new agents. They have laboratory facilities to do it and you buy kits over the counter. When you're a young high school student nothing looks as tough as it may appear to a 30 or 50 year old. And if you want some precedent of this, just think about hackers who are doing much the same thing with respect to our information technology infrastructure: how many of them are young kids still quite capable of mounting ferocious attacks and have the motivation to be playing those kinds of games. It's mostly a metaphor, but something to be taken somewhat seriously about where the technology is heading us.

Now why is high tech microbiology even more dangerous than natural disease? I used to teach that it wouldn't be. That the evolution of disease agent was very complicated, putting together all the things needed for a bug to adapt itself to the environment of a host, defeat its defense systems and so forth, would make it unlikely that you could synthesize a brand new pathogen even with quite deep bio-technical knowledge. And that is still true. But I've had further reflection. Consider the business of our natural infecting agents, the influenza that you'll get, the common cold, your boils, your gut infections, your staph on your skin and so on and so forth. Their economy is not to kill their host. But things happen. They happen as a byproduct of the skirmishing between them and host defenses. If you look around the world of infectious disease, in fact you find that with rare exceptions, our most lethal diseases are almost accidental byproducts of a bug moving away from its natural host. That's outstandingly true of HIV--AIDS which is in equilibrium with its primate hosts and doesn't cause an enormous amount of mischief there. It's jumped into humans just as plague has jumped into humans, just as Avian flu has jumped into humans, and there can have devastating results. But that's because evolution has worked in reverse direction. In their natural historical environment, most bugs are selected for moderated virulence, because they will survive better in that natural world if they don't kill the host. If they get past the outer skins, the beach head of our body, and lodge in it and stay put like tuberculosis does, but with only protracted disease, only with chronic infection as the outcome, just as long as the host is alive, the bugs can still survive within that host, they can continue to play the game of disseminating their genes, transferring infection to new hosts over and over and over again. So the bugs that would kill their host promptly, the acute infection, are in nature selected against. That's where technology should override that natural restraint, and if we were to see the importation of say, botulinum toxin, to a wide variety of other existing pathogens, we might find they would be far more lethal in a way that would be self-destructive to them (and to us) in their natural environment. But these would make even more horrendous kinds of weapons in the artificial circumstance of technical use. I've come to worry a lot about those kinds of innovations. There have been 2 or 3 published experiments down that line, in which anthrax has been used as a vehicle for importing still other toxins. Why would anyone do that? Well, anthrax is a well-adapted pathogen. Usually there's a local lesion; in cattle it's rarely that fatal. Even in humans you typically have a skin lesion from contact with an infected animal; it is a zoonosis carried over from another species. In its natural mode of transmission, it has a moderately low lethality. It's only when it is artificially disseminated by aerosols and by an inhalation portal of entry that it has the features we now recognize for BW. But by putting other toxins into anthrax, this stands a very good chance of defeating the vaccine that we have developed against this particular disease, and we are going to need a very different approach in vaccine design when it's not the natural anthrax toxin but the imported one.

On the other hand, in nature, where do we find botulinum toxin? It's the most potent toxin around by a factor of 100 or so compared to even other bacterial toxins. You don't see it in the ordinary pathogens that cause systemic disease. You see it in the bottom feeders: in the anaerobic bacteria that live in the bottom of lakes, or in sealed cans of food. The human body is a very unnatural part of its life cycle. The bottom of a lake is an anaerobic, non-air environment. That birds drop dead and fall into the lake and then sink to the bottom is part of the natural history of the botulinus organism. But that's not a typical infectious disease. We don't find the toxin in other pathogens, not because it couldn't migrate from species to species. We know very well that it could; there are biological mechanisms for it. But it's too hot to handle. It would be selected against very rapidly as a natural entity because of its high lethality--a rule that would be abrogated in intentional use. So there's a lot to worry about in the future.

The first few, the next few efforts at using biological weapons are very likely to be fumbles. I'm sure Bill Patrick has told you of the great difficulties there are in providing assured dissemination

on a very, very large scale. But unhappily that message is being heard often in the wrong quarters, and how-to-do it manuals in ways that approximate how to do it more effectively are becoming more and more visible as we go along. There will still be fumbles initially and I think it's very important that we do have a defensive infrastructure in place to assure that those first few events are fumbles, that they can be dealt with without a moderately small attack generating immense confusion, battling among the participants for who has the authority and the responsibility and lapses in preparedness that could readily convert a small fumble into a very large scale disaster.

But let me turn from that to where solutions might come from. I was happy I did come in time to hear Joseph Pilat and I echo very strongly a great deal of what he had to say, which is basically, we have to look at intentions as well as capabilities in this sphere. Try to understand them more deeply and try to modify them in various ways, and I'll try to take off on that in some very concrete fashion. This is to say, the capability of doing mischief for a very long time has greatly exceeded what has actually been done. BW has not in modern times reached the currency in formal warfare that chemical weapons did, as they did in WWI with a vengeance. The latter have always had to be thought about as being a battlefield military weapon as well as a strategic one and therefore present a very different set of problems than does BW. BW has been subject to restraints at various times. We don't understand them very well. We experience a very deep sense of moral revulsion and outright fear. Some of this comes from our understanding: you let that tiger loose, he's going to come back and eat you up as well. There's no limit as to what the eventual spread of BW will be. Both in the metaphorical sense in spreading the habit of using them, and in a very concrete sense. You know, let smallpox loose, you've made war against the world. That's why I'm really very skeptical about the notion that it was seriously thought of as a weapon to be used by other states against American cities. How in the world would it not spread to all the rest of the world if it established a beachhead in any population? That doesn't guarantee that some millennialist or someone who wants to kill the world thinks it's time that it happened! I'm very greatly relieved we had no major event on January 1, 2000. But watch out for 2001 which is when the next millennium really begins. A number of people share in some perplexity that the serpents didn't come crawling out of the woodwork on that first provocative occasion. Perhaps there was the right degree of publicity about defensive measures in place and so on. I'm not being totally reassuring, certainly not to myself in saying how bizarre it would be for anyone to apply some of the weapons that we would have the greatest concern about. It does narrow down the field of who's likely to use them. Getting a deeper understanding about those intentions, about what those barriers have been, are, and might be in the future, I think is a very important part of our agenda.

So what are some of the things that might strengthen those barriers or counter the erosion? We've made some very serious mistakes in the past. Above all, during the Cold War we continued our own offensive BW program for decades during a time when nobody in his right mind really believed we would ever use biological weapons. We never needed them. We had weapons perfectly capable of providing whatever level of deterrence or compellence we needed, and in a far more precisely targeted way than with BW. It became a little bit of a technological plaything. There was always that technological imperative, let's just try it! But it was never seriously thought through. If our own military had not understood Soviet doctrine, and had thought of BW on the offensive side as being directed primarily to our troops, that's a failure of vision we just have to attribute to the stresses of the Cold War. But I don't know what our own doctrine was for the conditions under which they would be applied. I half suggest it was a never very serious one. Now there are folks here from USAMRIID, alumni of the offensive program, may be able to fill us in on that, but we'll have to do that offline a little bit later on.

Overall, as President Nixon eventually recognized, it was very much against the national interest of this country to continue to fund major offensive programs over the years that we had them. That inevitably resulted in enhanced expertise about the building of these weapons and established a higher level of credibility for them. I think they did little about deterrence.

They did a great deal about provocation for similar efforts on the part of other parties. And they also left a cache of secrets that can't be kept silent that long, that deeply. Not 20, 30, 40 years: the promulgation of the core knowledge of what happened in the offensive program is part of what we are worrying about at this very moment with the prospects that they will be used against us. Well, happily we're past our own offensive BW programs. It was a very wise act on President Nixon's part to abjure them. He had little opposition from the chiefs at that time because they shared the views about the tactical disutility. I don't know what conversation there was about the strategic disutility of the program. And certainly leverage to get a highly flawed, but still better than nothing, BW disarmament convention was an equally important element. Now that convention has not worked to everybody's expectation. It did not greatly exceed mine, but I was greatly in favor of it because we have at least de-legitimated biological weapons. BW programs if they continue on the part of others, will have to be done under some cloak of secrecy and evasion, and we then have a lot of leverage about our own enforcement measures, about how we can mobilize world opinion and mobilize our own resolve in terms of responding to them. So even though the piece of paper, the treaty per se, has had some limited role in the eradication of these weapons, it was a necessary step if we are in fact to try to organize a no-BW regime for the rest of the world. We just need to be very realistic about how fast and how far we can go. The treaty needs to be reinforced by the inculcation of the resolve that we really mean it, and that we are going to take the measures necessary for its enforcement in the places that really count. Essentially on political grounds, I don't worry that Russia is going to use BW against the United States.

I do worry that there may be leakage from their programs to other countries. Either at official levels, or much more likely at unofficial ones of private individuals who otherwise don't know how to feed their families, going to sell themselves to the devil and provide material and some degree of insight and so on. That's a matter that's been widely discussed. We would be in a very poor position to take measures against that roguery if we did not have the treaty framework as a basis for de-legitimization of these kinds of weapons.

In the name of a myopic Realpolitik, we made another very grave error in our nonchalance about the Iraqi use of chemical weapons against Iran, against every standing convention on this matter. In public statements, well we kind of had a "tilt towards Iraq". We wanted to maintain a balance of power between Iraq and Iran. Some were happy to see them kill each other off and so let's overlook the longer-range values. I think we're reaping the whirlwind in that regard in trying to cope with Iraq's very large investment in that cognate technology.

Then there was some allusion to self-fulfilling prophecies, an allusion which I'm very much in accord with. The media dramatization, the very articulate advocates, the people spreading not totally illegitimate scare stories about how awful smallpox attack might be. The odds of smallpox ever being used have probably been enhanced by the amount of conversation that there has been about its possibilities, about our defenselessness, about our responses to it. I know we can't control the media. I do my best by staying out of it, but that's a very small item. And it is a dilemma to know just what the optimum policy is in that regard. One, we can't keep secrets of fact on that matter. Two, we certainly need some level of public discussion or there won't be any policy debate. But I still wince when I see these things on the banner headlines or the tabloids and I ask your own wisdom and forbearance to try to play it cool in that regard. I was very happy

to see the strategies that were mentioned with respect to the FBI and other agencies handling of the anthrax threats and the cooling down of the number of attacks of the hoaxes that have come along is a common sensible conclusion. Understanding that phenomenon more deeply (but don't ask me how we go about doing it), finding greater wisdom on the matter would be equally so.

I will be at risk of being called Polyanna, for referring to psycho-social, moral limitations to violence. In the current context, our own care as a nation in the execution of our national and military policy is nevertheless very important. We have to inculcate dignity and respect for this country and for its ideals -- not to exclude an appropriate level of fear and "watch out you'll be punished" if you misbehave. Especially if you misbehave in a context that violates the legitimate instincts of the rest of the world community. To the extent that in our own conduct, we neglect that care, to the extent that we're indifferent to collateral damage, we're encouraging the same kind of mentality that's involved in blowing anthrax and spreading smallpox. It legitimizes the use of violence against civilian populations as a reflection of how we as a nation exercise and justify the right to use that violence against others. Of course there are circumstances where that's absolutely unavoidable, but history has taught that violence begets violence and violence against civilians begets violence against civilians, even more particularly. We must learn to be smarter about it. The intentions are there, I'm not belying that. But such use of force remains very clumsy: and bombing is a very blunt instrument to try to achieve national policy. We just haven't developed sharper tools that can dissect the interests of a tyrant from those of his subjects. In any matter remotely connected with BW we must be especially careful to come with clean hands.

There are some positive steps. It is very important that we enhance the international consensus that BW is an evil that cannot be tolerated. It cannot be tolerated out of a sense of moral outrage, and of concern about our own welfare for sure, but it cannot be only our own survival. Civil life depends on the frustration of individuals' capacity to disrupt the entire community at a whim. If people can resort to maximum violence in settling their grievances, and this becomes habitual, we have no civil life any further. It's in that sense that these are weapons that our community cannot tolerate. And we have to install premonitory measures; we have to cooperate even against some of our other interests in order to deal with it. We have to be more sophisticated about our persuasion. Sometimes it means being less heavy handed in the way we operate in our policy in the international sphere with the aim of achieving that consensus and making it stick.

There is one program of a very positive kind that would reinforce it all, and would be a very great benefit to us directly as well. That is to be even more than we are, a major partner in our global attacks against infectious disease. That in this world today 7-800 million people are considerably damaged by malaria infection and 2 or 300 million with tuberculosis, and several million deaths a year from avoidable diseases; that even deployment of our existing technology could go a long way to alleviating that kind of distress. This has been commented from time to time, but I would say that we have been lackadaisical in our responsibilities to the global community about the recognition that infectious disease is a threat to the entire species. I don't say that sentimentally. I say that realistically, and to the extent that these diseases still flourish anywhere in the world, we're asking to be visited again with another HIV pandemic of the kind that we had over the last 20 years. There's a very direct connection between cooperation with other populations anywhere around the globe and our own survivability as we sit very comfortably behind our borders. These bugs don't recognize those borders. And it would be a very important part of the bargain that we are tacitly making with underdeveloped countries, who can't afford our sophisticated weapons. The non-proliferation regime says "look, if we're in this game together, you forego the biological weapons that might even the playing field from your point of view and we will continue to be part of that global effort to fight infectious disease as an enemy of all humankind." I know how

sentimental that sounds, but I also want to convey to you how practical and how important that is for your own survival.

Now I will also submit that there would be nothing more devastating to our security that a successful demonstration of the power of an attack with weapons of mass destruction. I do not in any way want to minimize the efforts at organization, at preparedness, at coordination, at anticipation, at intelligence, at warning that have been the main theme of this symposium. The first successful attack will not be the last one. And to the extent that the culprits can get away with it and demonstrate its power, they will be setting an example that will be ever more difficult to avert later on. So there's much, much more at stake than the casualties that might be involved in any single incident. We're really at a turning point in what the future history of biological weapons might be. Meetings like this at one level, the top-level coordination of efforts that Dick Clarke is going to be talking about tomorrow, are equally important towards that goal of containment. Thank you very much.

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#### Roles for infectious disease specialists

1. anticipation of threat agents and modalities of dissemination, and their public health impact.
2. assistance to local emergency authorities in planning for consequence management of a BW attack.
3. participating in local public health teams in the epidemiological investigation and definitive diagnosis of suspicious outbreaks.
4. as central agents in the medical and public health management of outbreaks, and of their further consequences for the life of the community.
5. assisting other branches of government in authentic assurance and guidance to the public, in averting panic and chaos.
6. where appropriate, assisting in measures to limit the further spread of contagious agents, and to decontaminate impacted facilities.
7. ongoing basic and translational research to sharpen the tools available for all these functions, and further training of colleagues and supporting personnel.
8. instilling a globally shared ethos in condemnation of any possible use of BW, or offensive planning and preparation therefor.